region remains at a consistently high level, but the detection rates of colon cancer in women have increased. Men were exposed to colorectal cancer more frequently than women, especially in the older age groups. Meanwhile the share of detection of colorectal cancer clinical stage 3–4 decreased by one third. With regard to liver cancer, decline was observed over 25 years that is 2.1 times lower that coincide with national trends. At the same time, death rates from liver cancer in Novosibirsk are lower than in Russia as a whole. However, the index of malignancy (the ratio of mortality to incidence) of liver cancer was 0.94 in Novosibirsk.

In summary, while there are a variety of long -term monitoring of trends in the incidence of cancer, this requires new research, especially the identification of genetic markers for the prevention and possible introduction in oncologic patients.

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Changes in peripheral blood lymphocyte subpopulations implicated in regulatory and cytotoxic immune reactions mirror the process of immunoediting in cervical pre-invasive cancer

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Background: The ability to promote an immunosuppressive microenvironment has been recognized as one of the "next generation" cancer hallmarks, being most apparent in case of HPV-induced carcinogenesis, since it is a prerequisite to the virus persistence and proliferation of keratinocytes expressing HPV-antigens. With respect to HPV-associated cervical cancer, it is commonly known that initial pre-cancerous intraepithelial lesions frequently undergo reverse development due to effective recognition and eradication by the immunocompetent cells. Both innate (e.g. NK) and adaptive (helper and cytotoxic O-cells) arms of immunity have been implicated in the regression of neoplastic cells, with NK T-cells considering as a connecting link between two branches. Progression of intraepithelial neoplasia leads to the establishment of pre-invasive cancer, which can be regarded as the result of a completed immunoediting of the tumor locus, because further, with 100% probability, it turns into invasive metastatic form. We assumed that the signs of immune activation, on the one hand, and the signs of immunosuppression, on the other hand, despite the locality of pre-invasive cervical cancer, can be found in the circulation and can be relevant to the development of tolerogenic microenvironment. The aim of the present work was to investigate the number of functionally different subpopulations of T- and NK-lymphocytes in the blood of patients with pre-invasive cervical cancer.

Material and methods: Blood samples were taken from 35 HPV (+) patients diagnosed with cancer in situ. The control group consisted of 30 healthy HPV(−) women with no pathology of the cervix. Lymphocytes were immunophenotyped by MACSQuant flow cytometer. The percentage of the following populations were measured: CD3+CD95+/high, CD3+CD4+, CD3+CD4+CD95+/high, CD3+CD8+, CD3+CD8+CD95+/high, CD4+CD25+, CD4+CD25high, CD4+CD25+CD127dim/neg, CD4+CD25+FoxP3+ (CD4 Tregs), CD8+CD25+, CD8+CD25+CD127dim/neg, CD8+CD25+FoxP3+ (CD8 Tregs), CD3−CD16+, CD3−CD56+, CD3−(CD16±)CD56bright, CD3−CD16+CD56+, CD3−CD16low/negCD56+, CD3−CD16+CD56- (NK subpopulations), CD3+CD56+, CD3+CD16+CD56+ (NK T-lymphocytes).

Results: Increase in the number of CD4 Tregs that are known to exert immunosuppressive effect was found in cancer patients' group, namely the increased quantity of cells with CD4+CD25+ (especially, CD4+CD25high fraction), CD4+CD25+CD127dim/neg, or CD4+CD25+FoxP3+ phenotypes was shown. At the same time, the portion of CD4+FoxP3+ lymphocytes didn't differ between the studied groups. A rare population of CD8+ Tregs (CD8+CD25 +CD127dim/negFoxP3+) also exhibited a tendency to accumulate in the blood of cancer patients compared with the control. Analysis of the major subpopulation of NK cells performing cytotoxic reactions didn't reveal significant difference between the examined groups. Similar result was obtained in relation to the other functional groups of NK cells, specifically CD3−CD16±CD56bright (cytokine-producing NKs with low cytotoxicity), CD3−CD16dim/−CD56+ (NKs with potential anti-tumor activity), and CD3−CD16+CD56 – (NKs associated with viral infection or NK-precursors). However, an increase of NK T-lymphocyte amounts was established, arguing both activation of anti-tumor response and its inhibition, in view of functional polymorphism of this population. Similarly, the increased number of CD3+CD95+/high cells and CD3+CD4+CD95+/high T-helpers may have dual significance, taking into account that the mid-early T-cell activation marker CD95/Fas presents the key death-receptor (earlier we have revealed the elevated activity of caspases involved in the Fas-mediated signaling in circulating lymphocytes of cervical cancer patients). The total numbers of CD3+CD4+ T-helpers and CD3+CD8+ T-killers were generally comparable between the groups analyzed, with T-killers displaying slightly decreased percentage in the patient group.

Conclusion: The processes supporting establishment of immunosuppressive microenvironment extend beyond the local level during the earliest steps of cervical cancer progression. The observed changes may reflect the shift of equilibrium between immune activation and suppression, which is the essence of immunoediting. Further phenotypic analysis of cell subpopulations reported here is required for understanding the functional meaning of these changes.

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Detection of HER2 mRNA splice variants in exosomes of breast cancer cells

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